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APPLICATION FOR U.S. LETTERS PATENT

Title:

PROCESS FOR MAKING GEL FILMS

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PROCESS FOR MAKING GEL FILMS

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Nos. 60/462,785; 60/462,721; 60/462,758; 60/462,617; 60/462,793; 60/462,783; 60/462,792; 60/462,794; all filed on April 14, 2003.

FIELD OF THE INVENTION

The present invention is directed to a process for making homogeneous, thermoreversible gel films comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a film forming composition in an apparatus providing sufficient shear, temperature and residence time to form a homogeneous molten composition, wherein the temperature is at or above the solubilizing temperature of said composition; (ii) feeding the molten composition into at least one of a mixer, pump or devolatilizer; and (iii) cooling the homogeneous molten composition at or below its gelling temperature to form said gel films. The present invention is also directed to various products made from such films, such as the gel films themselves, soft capsules, solid dosage forms and delivery systems.

BACKGROUND OF THE INVENTION

It is known that certain high solids, low moisture film forming compositions containing, for example, hydrocolloids, form highly viscous solutions that make

formation of hydrated films difficult to obtain. The present invention provides a process for preparing high solids, low moisture films from such highly viscous solutions.

In addition, many attempts have been made to make soft capsules from high solids, low moisture films such as hydrocolloids. However, such attempts to make soft capsules have suffered from the drawback mentioned above. That is, hydrocolloids are known to form highly viscous solutions that are difficult to sufficiently hydrate and form a film in conventional soft capsule making processes. The process of the invention therefore allows for the manufacture of soft capsules from such films.

SUMMARY OF THE INVENTION

As a first embodiment, the present invention is directed to a process for making homogeneous, thermoreversible gel films comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a re film forming composition in an apparatus providing sufficient shear, temperature and residence time to form a homogeneous molten composition, wherein the temperature is at or above the solubilizing temperature of said composition; (ii) feeding the molten composition into at least one of a mixer, pump or devolatilizer; and (iii) cooling the homogeneous molten composition at or below its gelling temperature to form said gel films.

As a second embodiment, the present invention is directed to the homogeneous, thermoreversible, gel films made from the above process.

As a third embodiment, the present invention is directed to a process for making soft capsules comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a film forming composition in an apparatus providing sufficient

shear, temperature and residence time to form a homogeneous molten composition, wherein the temperature is at or above the solubilizing temperature of the composition; (ii) feeding the molten composition into at least one of a mixer, pump or devolatilizer; (iii) cooling the molten composition to or below the solubilizing temperature of the molten composition to form the homogeneous, thermoreversible gel film; and (iii) making soft capsules from the gel film.

As a fourth embodiment, the present invention is directed to soft capsules made by the above process.

As a fifth embodiment, the present invention is directed to a process for making a solid dosage form comprising a fill material encapsulated by a homogeneous, thermoreversible gel film comprising the steps of: (i) preparing the homogeneous, thermoreversible gel film in accordance with the above process; and (ii) encapsulating the fill material in the gel film. The present invention is also directed to solid dosage forms made from the process.

As a sixth embodiment, the present invention is directed to a process for preparing a homogeneous gel film delivery system comprising an active substance and a homogeneous, thermoreversible gel film, comprising the steps of: (i) preparing the molten composition in the above process; (ii) adding an effective amount of an active substance prior to or after formation of the molten composition: and (iii) cooling the molten composition containing the active substance at or below its gelling temperature to form the gel films containing the active substance. The present invention is also directed to delivery systems made by the process.

As a seventh embodiment, the present invention is directed to a process for making homogeneous, thermoreversible gel films comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally de-aerating a film forming composition in an apparatus providing sufficient shear, temperature and residence time to form a homogeneous molten composition, wherein the temperature is at or above the solubilizing temperature of the composition; and (ii) cooling the homogeneous molten composition at or below its gelling temperature to form said gel films. The present invention is also directed to dosage forms, solid forms and delivery systems made by the process.

DESCRIPTION OF THE FIGURES

Figure 1 is schematic of a process of the present invention to make films and soft capsules using a Stephan processor together with an extruder. The extruder is optional in this figure, and the Stephan processor can be replaced with, e.g., a Ross mixer. Further, while this figure refers to "LV Guar" (low viscosity guar), this invention is not limited thereby.

Figure 2 is a schematic of a process of the present invention to make films and soft capsules using a fluid mixing apparatus such as in Figure 3 together with an extruder. The extruder is optional in this figure.

Figure 3 is a partially broken away, side elevational view of the fluid mixing apparatus for mixing first and second fluids with steam that can be used in the process of Figure 2.

Figure 4 is another version of the schematic of Figure 2 showing the film coming out of the extruder proceeding to an encapsulation apparatus.

DETAILED DESCRIPTION OF THE INVENTION

A first embodiment of the present invention is a process for making homogeneous, thermoreversible gel films comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a film forming composition in an apparatus capable of providing sufficient shear, temperature and residence time to form a molten composition, wherein the temperature of the molten mass is maintained at or above its solubilizing temperature; (ii) feeding said molten composition into at least one of a mixer, pump or devolatilizer; and (iii) cooling said molten composition at or below is gelling temperature to form said gel films.

The process of the present invention provides homogeneous, thermoreversible gel films having, e.g., a relatively high solids content.

As used herein, "homogeneous film" defines films that, to the naked eye, are visually uniform and free of defects such as lumps, cracks, particles that are undissolved that should be dissolved, non-uniform distribution of insoluble particles, etc. "Fish eyes" (mixed liquid and solid states) or "gel balls" (non-uniform gel structure) would not meet the definition of "homogeneous" as used herein.

The gel films of the present invention are homogeneous, thermoreversible gel films. They can be cast and used in a variety of applications as cast films or in further processing.

As used herein, "thermoreversible film" defines a film that has a melting temperature. As used herein, the melting temperature is the temperature or temperature range over which the gel film softens or flows.

As used herein, the phrase "gel films" refer to a thin membrane formed from, e.g., structured hydrocolloid. The gel-forming composition is characterized by a gel temperature, the temperature below which the molten mass of the gel composition must be cooled to form a self-supporting structure. Optionally, a molten mass can be cast hot and allowed to cool, as well as dry to further concentrate the solids (controlled moisture removal) until a gel film is formed by the gel composition. The melt temperature of a thermoreversible gel film is higher than its gel temperature.

As used herein, the "solubilizing temperature" means the temperature at which the composition becomes homogeneous. Solubilizing refers to the act of fully dissolving all the soluble components in the molten composition and all insoluble materials are uniformly dispersed.

The components in the film forming system can be any components found in film forming compositions that form high solids, low moisture gel films when heated and hydrated and that form homogeneous, thermoreversible gel films. For example, such compositions can contain thermoreversible hydrocolloids.

The thermoreversible hydrocolloids that can be used in the present invention to form thermoreversible gel films include polysaccharides such as: carrageenan including iota carrageenan, kappa carrageenan, kappa-2 carrageenan; xanthan gum; polymannan gums (e.g., glucomannan gums and galactomannan gums) such as locust bean gum, konjac, tara gum, cassia gum, guar gum (e.g. low viscosity guar gum); alginates including

propylene glycol alginate and monovalent salts of alginates such as potassium and sodium; pullulan; gellan (including high and low-acyl gellan); dextran; pectin and combinations thereof. The carrageenans can be modified, less than fully modified or unmodified. As used herein, kappa-2 carrageenan has a molar ratio of 3:6-anhydrogalactose-2-sulfate (3:6-AG-2-S) to 3:6-anhydroglactose (3:6-AG) content of 25 to 50%, iota carrageenan has a molar ratio of 3:6AG-2S to 3:6AG content of 80 to 100% and kappa carrageenan has a molar ratio of 3:6AG-2S to 3:6AG content less than that for kappa-2 carrageenan. For example, kappa carrageenan from *Eucheuma cottonii*, a commonly known and used seaweed source for kappa carrageenan, has a molar ratio of 3:6AG2-S to 3:6AG content of less than about 10%; and iota carrageenan from *Spinosum*, a commonly known and used seaweed source for iota carrageenan, has a molar ratio of 3:6AG2-S to 3:6AG content greater than about 85%. This means that kappa-2 carrageenan comprises a ratio of kappa (3:6-AG) repeating units to iota (3:6-AG-2-S) repeating units between 1.0 to 3.0:1, more particularly, 1.5 to 3.0:1 (more particularly depending on the desired application). The molar ratio of 3:6AG-2S to 3:6AG content in these carrageenans holds regardless of its degree of modification and precursor content (e.g, mu and nu repeating units).

The homogeneous, thermoreversible gel film made by the process of the present invention can optionally contain at least one of a plasticizer, a second film former, a bulking agent and a pH controlling agent depending on their application.

Examples of such a plasticizer include polyols such as glycerin, sorbitol, maltitol, lactitol, corn starch, fructose, polydextrose, solubilized oils and polyalkylene glycols such as propylene glycol and polyethylene glycol. For example, such plasticizers can

generally be used in an amount of at least 5%, more preferably, at least 10%, more preferably, at least 20%, more preferably, at least 30% by weight of all the components including water in the dry film if a gel film having more elasticity is desired; e.g., films to be used to make soft capsules. For other applications, such as hard capsules, where less elastic films are desired, the plasticizer can be present in an amount of 0% to 20% by weight of all the components in the dry film. It is possible that the gel film of the invention contains no plasticizer at all. If desired, where iota, kappa or kappa-2 carrageenan is used as the hydrocolloid, such carrageenan can have a viscosity of 19 cps or less, more particularly less than 10 cps, at 75 °C when measured 0.10 molar sodium chloride solution containing 1.5% of such carrageenan by weight based on the total weight of the composition. This viscosity test can be performed using a Brookfield LVF (Brookfield Engineering Laboratories, Inc.) viscometer using Spindle #1 at 60 r.p.m. and determining the viscosity after six revolutions.

Examples of the second film former that can be used in the present invention include at least one of a starch, starch derivative, starch hydrozylate, cellulose gum, hydrocolloid, an alkylcellulose ether or a modified alkyl cellulose ether. Examples of the hydrocolloids are those listed above. Others include non-gelling carrageenans such as lambda carrageenan. An example of an alkylcellulose ether that can be used in the present invention is hydroxyethylcellulose. Examples of modified alkylcellulose ethers that can be used in the present invention include hydroxypropylcellulose and hydroxypropylmethylcellulose. The primary film former can be the only film former in the gel film. When the gel films of the present invention contain second film formers, the

primary film former can be present in an amount of at least 10%, at least 40%, at least 60% or at least 80% by weight of the total amount of film formers in the gel film.

Examples of the bulking agent include microcrystalline cellulose, microcrystalline starch, modified and unmodified starch, starch derivatives, inulin, starch hydrozylates, sugar, corn syrup and polydextrose. As used herein and in the claims, the term "modified starch" includes such starches as hydroxypropylated starches, acid-thinned starches, and the like. Examples of modified starches that can be used in the present invention include Pure Cote™ B760, B790, B793, B795, M250 and M180, Pure-Dent™ B890 and Pure-Set™ B965, all available from Grain Processing Corporation of Muscatine, Iowa, and C AraTex™ 75701, available from Cerestar, Inc. Examples of starch hydrozylates include maltodextrin also known as dextrin. Unmodified starches such as potato starch can also contribute to the film strength when combined with the hydrocolloids within the scope of the invention. In general, modified starches are products prepared by the chemical treatment of starches, for example, acid treatment starches, enzyme treatment starches, oxidized starches, cross-bonding starches, and other starch derivatives. It is preferred that the modified starches be derivatized wherein side chains are modified with hydrophilic or hydrophobic groups to thereby form a more complicated structure with a strong interaction between side chains.

The amount of the bulking agent to be used in the present invention is generally in the amount of 0 to 20% by weight of the dry film, but more can be used, if desired, for example, at least 20%, more preferably, at least 30% of the dry film depending on the application.

Note that starch, starch derivatives and starch hydrozylates can be multifunctional. That is, in addition to being used as bulking agents, they can be used as second film formers. When such are used as bulking agents and second film formers, they are generally used in an amount of at least 10%, preferably, at least 20%, by weight of the gel film.

Examples of the pH controlling agent to be used in the present invention include bases such as hydroxides, carbonates, citrates and phosphates. The pH controlling agent can be chosen as the source of added beneficial cations such as potassium. For some compositions, the pH controlling agent can be used to improve the stability of the gel film. The amount of the pH controlling agent is generally in the amount of 0 to 4%, preferably, 0 to 2%.

The dry films made from the gels of the present invention have been found to have, for example, a break force of at least at least 1,000 grams, at least 2,500 grams, at least 4,000 grams, at least 5,000 grams, at least 6,000 grams, as determined by using a Texture Analyzer TA-108S Mini Film Test Rig. In some cases, wet films made by the process of the present invention have yielded low break force strength (e.g., 250-320g), but have produced strong dried films having the break force strengths mentioned above.

The gel films of the present invention have been found to have a solids content of at least 50%, at least 60%, at least 70%, at least 80% and at least 90% of all components in the gel film. It is understood that up to 15%, 10%, 5% water may remain strongly associated with the solids in the gel film.

Dry film thicknesses generally used for soft capsules are in the range of 0.5 to 3.0mm, more preferably, 0.8 to 1.2 mm.

It is possible that the films of the present invention can contain nonthermoreversible gums. However, so as not to adversely impact the homogeneous and thermoreversible nature of the gel films of the present invention, such nonthermoreversible gums should be present in an amount of less than 50% by weight of the thermoreversible film former, preferably, less than 40% more preferably, less than 30%. Examples of such nonthermoreversible gums include crosslinked or partially crosslinked gums such as calcium set (e.g., crosslinked) pectins or alginates. Calcium reactive alginates and pectins, as well as their less refined forms, are considered as thermoreversible gums in the absence of divalent cations.

The gel films of the present invention are generally made from a process utilizing an apparatus that enables sufficiently high shear, temperature (above the gelling temperature) and residence time so as to provide a homogeneous molten mass of the composition and formation of the gel upon cooling. This is generally accomplished in the apparatus by heating, hydrating, mixing, solubilizing and optionally de-aerating the composition. Such apparatus include but are not limited to Ross mixers, Stephan processors, conventional jet cookers, extruders and the fluid mixing apparatus as set forth in Figure 3. Ross mixers, Stephan processors, extruders and conventional jet cookers are readily available commercially. Prior to cooling, the molten mass can be fed to at least one of a pump, mixer or devolatilizer. An example of a device that performs any one of such functions is an extruder. An extruded molten mass can also be directed to a film forming or shaping device (e.g. spreader box, as used in a capsule forming machine) that aids in the uniform casting of a continuous film, or, through a die that allows a direct formation of a film from the molten mass delivery equipment. Care must be taken to

maintain the molten mass above the initiation of restricted flow/gel structure formation. Insulated and pre-heated (to maintain proper temperatures) transfer hoses may be used to insure molten mass flow until desired gel film formation is initiated on the casting rolls or at other film formation points, such as an extruder (restrictive flow, film forming device) or die. Additional processing methods (such as pre-heating the discharge/plunger-like head as seen in a Ross process system) can force (by pressure) the molten mass through the transfer hoses mentioned above. Additional insulation can help maintain molten mass temperatures through the use of a Teflon disk initially placed upon the molten mass surface immediately after removing the mixing device. In addition, the feeder hoses can be introduced to the heat controlled molten mass feeder (casting) boxes located on a capsule machine either directly to the boxes or through an optional modification of the feeder boxes which introduces a top half enclosure/cover that helps maintain molten mass temperatures within the feeder box, reduces moisture loss, and maintains uniform (center) filling of the box during the extended process of forming films for capsules. It is understood that other methods of maintaining molten mass temperatures can be used to form films for capsules. This includes, but is not limited to extrusion of the molten mass through dies/orifices into films that: can be immediately fed into the capsule forming apparatus, stored at temperatures that maintain proper film conditions (to form capsules) until needed, or dried to desired moisture, solids and texture levels, until needed. Such dried films have the property of re-absorbing water (water is introduced by any means) throughout its gel film matrix and can be rehydrated when needed, for example, to make soft capsules or other solid forms. Moisture is introduced to the film until a desired

moisture content and strength/texture is reached that will allow the film's introduction into a capsule machine to make soft capsules.

When a Stephan processor or conventional jet cooker is used, a typical process for using such with hydrocolloids is as follows. The components of the film forming composition are fed into the Stephan processor and heated (while agitating) to a temperature, which provides solubility to the components above their gel temperature. The material can then be processed into a gel film or as a molten mass. Further processing can be completed on this material while utilizing appropriate equipment to allow it to develop its final form.

As used herein, a "fluid mixing apparatus" refers to the apparatus in FIG. 3. FIG. 3 illustrates a fluid mixing apparatus **10**. The fluid mixing apparatus **10** is arranged to mix steam **2** with a first fluid or slurry **4** and a second fluid or slurry **6** to produce a molten mass or slurry mixture **8**.

The fluid mixing apparatus **10** comprises a first housing **20** having a first inlet **22** through which the steam **2** enters the housing **22**, a nozzle end **24** from which the steam **2** exits the housing **20**, and a nozzle valve or stem **26** disposed at the nozzle end **24**. An actuator means **30** is connected to the first housing **20** for controlling the exit rate or exit pressure of the first fluid **2** at the nozzle end **24**. The actuator means **30** may be of the type manufactured by Fisher Controls U.S.A.

The fluid mixing apparatus **10** further comprises a second, mixing housing **40** coupled to the first housing **20** at the nozzle end **24** of the first housing **20**. The second housing **40** includes a second inlet **42** through which the first fluid **4** enters the second housing **40**, and a third inlet **44** through which the second fluid **6** enters the second

housing **40**. The inlets **42** and **44** are disposed downstream of the first inlet **22**. As shown in FIG. 3, the second inlet **42** and third inlet **44** are disposed in a common plane and spaced apart radially from each other, most preferably directly opposite (i.e., 180° apart) about the central axis **Y** of the mixing apparatus **10**. The second housing **40** defines a generally cylindrical mixing chamber **52** that in turn defines a flow passage extending along the axial length of the mixing chamber **52** from an entry end **54** of the mixing chamber **52** to an exit end **56** of the chamber **52**. The nozzle valve **26** is movable by the actuator **30** between seated and unseated positions at the entry end **54** to control the flow rate of steam **2** into the mixing chamber **52**.

The nozzle end **24** of the first housing **20** directs the steam **2** into the entry end **54** of the mixing chamber **52**. The second inlet **42** and the third inlet **44** radially direct the first fluid **4** and second fluid **6**, respectively, into the mixing chamber **52**. The steam **2**, first fluid **4** and second fluid **6** are mixed in the mixing chamber **52** to form a molten mass or mixture **8** which exits the mixing chamber **52**. The molten mass **8** then may be shaped into a shaped article or formed into a film, such as by casting the mixture **8** onto a cooling drum or by passing the mixture **8** through an extruder.

Once the molten mass composition is prepared and such is maintained at a temperature at or above the solubilizing temperature, the molten mass may be then fed directly into at least one of a pump, mixer or devolatilizer. Then, the molten mass is cooled down to or below the gelling temperature of the composition to form the gel film.

It is preferred that the solubilizing temperature be greater than the boiling point of the homogeneous molten composition at atmospheric pressure and that the heating, hydrating, mixing and solubilizing is conducted above atmospheric pressure.

A preferred process comprises feeding the molten composition directly into a mixer, deareated, depressurized and pumped prior to cooling to or below the molten composition's gelling temperature.

One device that contains at least one of a pump, mixer and devolatilizer is an extruder. An extruder is preferred device for devolatilizing and thereby concentrating the solids of the molten composition prior to cooling.

Extruders that can be used in the present invention include single or dual barrel extruders with inlet devices sufficient to allow transfer of the fully or partially hydrated composition without incurring a temperature drop during the transfer. Once the compositional material achieves its targeted solids content and the temperature is maintained above its gel temperature, the resulting molten mass can be used as previously described.

As another aspect of the invention, it is noted that the molten mass need not necessarily reach homogeneity in step (i). That is, homogeneity of the molten mass can be obtained prior to or after feeding the molten composition into at least one of the mixer, pump or devolatilizer provided the molten mass reaches homogeneity prior to gelling.

Since the gel films of the present invention have been shown to have dry film strengths, e.g., of at least 2,500 grams, they are well suited for a variety of applications. For example, such gel films can be used to make soft capsules. Thus, as a second embodiment, the present invention is a process for making soft capsules comprising the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating the film forming composition in the apparatus capable of providing sufficient shear, temperature and residence time to form a molten composition, wherein the temperature is at or above

the solubilizing temperature of the molten mass; (ii) feeding the molten composition into an extruder to form a high solids, low moisture, homogeneous, thermoreversible gel film; and (iii) making soft capsules from the gel film. The gel film and its components, as well as the apparatus and extruder that can be used, are as set forth above.

The process for making soft capsules of the invention includes the use of any conventional encapsulating apparatus once the gel films discussed are prepared, e.g., a conventional rotary die apparatus or concave stamping die. For example, once the molten mass of the present invention has been made, it can be cast onto drums, cooled and then fed between rotary encapsulation dies where the films are heated again, filled, sealed and cut. For a good description of this conventional process, see WO 98/42294. Alternatively, and as a benefit of the present invention over conventional soft capsule processes, the use of the high shear apparatus disclosed above allows the molten mass to be sufficiently hydrated, extruded, applied to drums as they are cooling and then fed into conventional encapsulating apparatus for filling, sealing and cutting. This continuous type process can be used to eliminate the step of having to reheat fully gelled and cooled films for capsule preparation.

Other applications of the gel films of the present invention include process for making a solid form comprising a fill material encapsulated by the homogeneous, thermoreversible gel film of the present invention. One type of such solid form is a hard capsule. Hard capsules, as used herein, refer to those solid forms that are conventionally used, e.g., in the pharmaceutical industry whereby two half shells are formed, a fill material, usually a powder, is placed in the shells and the two halves are placed together to form the hard capsule. The process for making such hard capsules would typically

involve dipping metal pins or bars into the molten composition of the present invention and allowing the gel film to form around the pins. The gel films are dried and then removed from the pins. These processes are well known in the industry as methods of making hard capsules. The fill materials for the hard capsules can be any fill materials commonly used in such dosage forms. Generally, the fill materials can be liquids or solids such as powders. The fill materials can be a pharmaceutical ingredient, agricultural ingredient, nutraceutical ingredient, veterinary ingredient, food, cosmetic ingredient, flavorant, etc.

The solid form may also encapsulate a powder, tablet, caplet, microcapsule or capsule in accordance with known techniques. For example, encapsulating a hard capsule with the gel film of the invention would allow for safety seal/tamper resistant capabilities.

The gel film can also be used to modify the dissolution profile of the dosage forms. For example, gel films of the invention can contain added components that can create solid dosage forms having immediate release, controlled, enteric or delayed release capabilities. Definitions of "immediate release", "delayed release" and "enteric" can be found in the U.S. Pharmacopeia and are incorporated herein by reference.

In addition, the gel films of the present invention can be used in a process for preparing a homogeneous gel film delivery system comprising an active substance and a homogeneous, thermoreversible gel film, comprising the steps of: (i) preparing the molten composition; (ii) adding an effective amount of an active substance thereto; and (iii) cooling said molten composition containing said active substance at or below its gelling temperature to form said gel films containing said active substance. The active

substance can include at least one of an oral care agent, a breath freshening agent, a pharmaceutical agent, a nutraceutical agent, a salivary stimulant agent, a vitamin, a mineral, a coloring agent, a sweetener, a flavorant, a fragrance, a food.

Process for making homogeneous, thermoreversible gel films of the present invention also comprises the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a film forming composition in an apparatus providing sufficient shear, temperature and residence time to form a homogeneous molten composition, wherein the temperature is at or above the solubilizing temperature of the composition; and (ii) cooling the homogeneous molten composition at or below its gelling temperature to form said gel films. This process can be used to make dosage forms, solid forms and delivery systems as mentioned above. An apparatus especially suited for this process is the Ross mixer and, when making soft or hard capsules, can be used to provide the gel film directly to the capsule making machine or, if desired, to rollers for use at a later time. All of the materials described herein can be used in this process.

The present invention is now described in more detail by reference to the following examples, but it should be understood that the invention is not construed as being limited thereto. Unless otherwise indicated herein, all parts, percents, ratios and the like are by weight.

EXAMPLES

Example 1

The following example uses the fluid mixing apparatus of FIG. 3 to make the gel films of the present invention. In this example, Parts A and Parts B were pumped from

separate holding tanks at ambient temperature, as two separate streams **4, 6**, into two different inlet ports **42, 44** which fed the steam injection fluid mixing apparatus device **10**. The two individual streams **4, 6** were combined at the interface of the steam in the mixing zone **52** of the fluid mixing apparatus **10**. The separate solutions of Part A and Part B were readily pumped into the fluid mixing apparatus **10** and mixed with steam **2**. The steam **2** was introduced to the mixing zone at a pressure of 120 psi. The resulting molten mass or slurry mixture **8** flowed out of the exit port **56** of the fluid mixing apparatus **10**. The mixture **8** was poured onto a smooth surface and drawn down to form a homogeneous film **9**.

To measure the viscosity of the mixture **8**, approximately 500 ml sample of the mixture **8** was collected from the outlet **56** and poured into a jar. The temperature, pH and viscosity were measured for this sample at 95°C. A Brookfield LVF viscometer was used to measure the viscosity. An appropriate speed and spindle combination were used such that a reading could be taken. The dial reading was converted to dynamic viscosity (cP).

To measure the film strength and solids level, the molten mass **8** was collected from the outlet **56** then cast using a draw down bar, with a gap set at 3 mm, onto a stainless steel metal plate. The initial films **9** or "fresh films" were collected. Portions of the fresh films **9** were dried by placing them in a 40°C forced air oven. Break force was measured on the cast and dried film strips using a Texture Analyzer TA-108S Mini Film Test Rig. The percent solids were determined by measuring the difference between the initial weight of the fresh film and the final weight of the dried films.

To measure the gel temperature, a portion of the molten mass **8** was collected from the outlet **56** of the mixing apparatus **10** and transferred to a test tube. Half of the test tube remained empty. A glass thermometer was inserted into the molten mass **8**. The material **8** was allowed to cool under room temperature conditions. After each degree of cooling, the thermometer was removed from the material **8**. When a small, temporary indentation was observed in the surface of the mass **8**, this temperature was recorded. The thermometer was re-inserted into the mass **8**, which was allowed to cool further. The thermometer was removed and re-inserted at every degree of cooling until such a time as a permanent indentation formed in the mass **8**, such that the indentation did not refill. The temperature at which the permanent indentation formed was recorded. The gel temperature reported was the range between the two recorded temperatures. The components in the Tables below are further defined below in Tables 5 and 6.

Table 1 - Mixtures Containing Carrageenan

Example No.	1A	1B	1C	1D	1E
Part A (%)					
Carrageenan D	0.0	0.0	0.0	0.0	8.9
Carrageenan C	7.0	8.4	8.9	0.0	0.0
Carrageenan B	0.0	0.0	0.0	8.9	0.0
Glycerin	26.5	31.8	33.5	33.5	33.5
Part B (%)					
Starch	16.4	19.7	20.7	20.7	20.7
Water	50.0	40.0	36.9	36.9	36.9
Mixing chamber temp. (°C)	107	107	108	108	108
Outlet temp (°C)	101	102	102	102	102
Viscosity cP (@95°C)	7300	5200	48000	50000	12400
pH	7.3	Not tested	8	6.4	6.7
% solids	53	54	65	61	53
Gel temp. (°C)	46-50	43-47	53-60	80-85	49-52
wet film strength (grams)	267	214	983	2693	975
dry film strength (grams)	2958	6798	4594	6457	7017
Avg film thickness (mm) (%solids)			1.3 (74%) 1.7 (59%)		

Table 2 - Mixtures Containing Propylene Glycol Alginate

Example No.	2A	2B	2C	2D	2E
Part A (%)					
Carrageenan C	2.7	3.2	3.2	4.0	0.0
Carrageenan B	0.0	0.0	0.0	0.0	4.0
PGA	3.3	3.9	3.9	4.9	4.9
Glycerin	22.4	26.5	26.5	33.5	33.5
Part B (%)					
KOH	0.0	0.0	0.1	0.0	0.0
K_2CO_3	0.0	0.0	0.0	0.3	0.3
Starch	13.9	16.4	16.4	20.7	20.7
Water	57.8	50.0	49.9	36.6	36.6
Mixing chamber temp. (°C)	108	107	108	107	108
Outlet temp (°C)	102	102	102	101	102
Viscosity cP (@95°C)	5500	4650	2200	12400	9400
pH	4.1	4.2	8.7	6.3	6.8
% solids	48	50	not tested	58	57
Gel temp. (°C)	35-40	not tested	not tested	58-66	63-71

wet film strength (grams)	60	117	not tested	337	822
dry film strength (grams)	2408	3069	4335	4561	4795
Avg film thickness (mm) (%solids)				1.2 (91%) 1.1 (57%)	

Table 2 shows that the film former can be a combination of hydrocolloids, such as carrageenan and PGA. Additionally, salts can be added to influence film properties such as strength, gel temperature and pH.

Table 3 - Mixtures Containing Low Viscosity Guar

Example No.	**3A**	**3B**	**3C**
Part A (%)			
Carrageenan E	0	4.0	4.2
Carrageenan B	4.3	0.0	0.0
ULV guar	4.6	4.9	5.1
Glycerin	33.5	33.5	27.0
Sorbitol	0.0	0.0	8.1
Part B (%)			
Starch	20.7	20.7	21.8
Water			
Mixing chamber temp. (°C)	108	108	108
Outlet temp (°C)	102	102	102
Viscosity cP (@95°C)	7900	7800	69000
pH	6.5	5.6	5.5
% solids	57	57	55
Gel temp. (°C)	60-65	>100	>100
wet film strength (grams)	460	3402	921
dry film strength (grams)	5299	6587	9234

Table 3 shows that the film former can be a combination of hydrocolloids such as carrageenan and guar.

Table 4 - Mixtures Containing PES

Example No.	4A	4B
Part A (%)		
Carrageenan G	0.0	8.9
Carrageenan F	8.9	0.0
Glycerin	33.5	33.5
Part B (%)		
Starch B790	20.7	20.7
Water	36.9	36.9
Mixing chamber temp. (°C)	108	108
Outlet temp (°C)	102	102
Viscosity cP (@95°C)	>100K	8400
PH	7.5	8
% solids	46	49
Gel temp. (°C)	>100	>100
wet film strength (grams)	722	360
dry film strength (grams)	1095	4213

Table 4 illustrates that PES and upgraded PES can be processed in the mixing apparatus **10**. The upgraded PES provides some advantages, such as a lower outlet viscosity, and results in a higher strength dry film. The following Tables 5 and 6 provide further descriptions of the components specified in this Example.

Table 5 - Component Descriptions

Name	Trade Name	Supplier	Description
Gelatin		Kind and Knox	150 Bloom, Type B
Propylene glycol alginate (PGA)	Protanal BV 4830	FMC Corporation	
low viscosity guar (LV guar)	Edicol ULV 50	Indian Gum Industries, Ltd.	
Glycerin		Callahan Chemical	99.70%
Sorbitol	Sorbo	SPI Polyols	70% sorbitol solution, USP/FCC
Starch	Pure-Cote B790	Grain Processing Corporation	

Table 6 - Carrageenan Descriptions

Reference	Carrageenan Type	Description	Supplier
Carrageenan A	Iota	An alkali processed, clarified iota-carrageenan extract of *Eucheuma denticulatum* (*Eucheuma spinosum*) with low divalency	FMC Corporation
Carrageenan B	Kappa	An alkali processed, clarified kappa-carrageenan extract of *Kappaphycus alverezii* (*Eucheuma cottonii*) with low divalency	FMC Corporation
Carrageenan C	Kappa-2	An alkali processed, clarified, low divalency extract of a mixture of *Gigartina skottsbergii* and *Sarcothalia crispata*, primarily haploid (gametophyte) plants, such extract being commonly known as "kappa-2 carrageenan". Includes about 10-20% (total) of lambda and theta-carrageenans from diploid (tetrasporophyte) plants. Defined as the natural random block copolymer of kappa- and iota- in the ratio of about 1.0 to 3.0:1 respectively, and has significantly different functionalities compared to mixing individual kappa and iota-carrageenan natural polymers at the same ratio.	FMC Corporation
Carrageenan D	Very low divalent Kappa	An alkali processed, clarified kappa-carrageenan extract of *Kappaphycus alverezii* (*Eucheuma cottonii*) converted to the pure sodium salt with divalent cations removed.	FMC Corporation
Carrageenan E	Low divalent Kappa-2	An alkali processed, clarified, low divalency extract of *Gigartina skottsbergii*, essentially haploid (gametophyte) plants, such extract being commonly known	FMC Corporation

		as "kappa-2 carrageenan". Also includes minor levels (under 5% total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants. Defined as the natural random block copolymer of kappa- and iota -carrageenans in the ratio of about 1.0 to 3.0:1 respectively, and has significantly different functionalities compared to mixing individual kappa- and iota-carrageenan natural polymers at the same ratio.	
Carrageenan F	PES Kappa	An alkali processed, non-clarified, processed *Eucheuma* seaweed product (containing kappa-carrageenan) of *Kappaphycus alverezii* (*Eucheuma cottonii*) with low divalency.	FMC Corporation
Carrageenan G	upgraded PES Kappa	An alkali processed, non-clarified, pre-gelatinized kappa-carrageenan extract of *Kappaphycus alverezii* (*Eucheuma cottonii*) with low divalency, prepared as per example 5 in US Patent 6,479,649	FMC Corporation

As described and demonstrated above, the films made in accordance with this invention can be used in conventional capsule making equipment previously used for making gelatin capsules.

Procedures for Examples 2-7

Unless otherwise indicated, the following procedures were used to prepare and evaluate the materials and films in Examples 2-7. The Stephan UMC5 processor is a

laboratory scale-mixing device which provided suitable high shear mixing, heating, and deaerating of the formulations which were cast as films in the laboratory. A suitable batch size used with the Stephan UMC5 processor was 1500 grams.

An aqueous starch dispersion was prepared by dissolving any salts/buffers and pH modifiers in deionized water. The starch and/or maltodextrin (M100) were added and mixed until dissolved/dispersed. Pure Cote® B760 and B790 starches are available from the Grain Processing Corporation of Muscatine, Iowa.

A hydrocolloid mixture was prepared in the Stephan UMC5 processor by premixing the plasticizers until uniform, and adding the preblended dry hydrocolloids portionwise while mixing for about 30 seconds at 200 rpm after each addition. Sorbitol Special and glycerin were used as plasticizers. Sorbitol Special is an aqueous solution of sorbitol and sorbitol anhydrides at 76% solids supplied by SPI Polyols, Inc. (New Castle, DE).

The starch dispersion was added to the non-aqueous hydrocolloid mixture and mixed at 300 rpm for 5 minutes. The mechanical agitation was increased to 2100 rpm and the mixture was heated to 85°C to 95°C with mixing. When the target temperature was achieved, the mixture was stirred for 30 minutes, then the sample was held under vacuum (50-60 bars) with continued agitation for an additional 45 minutes.

When the hold time under vacuum at temperature has been completed, the sample was poured into a preheated wide mouth quart Mason jar. Temperature and pH were recorded. Viscosity was measured on the hot sample using a Brookfield LVF viscometer.

A small portion of the sample was set aside and refrigerated usually overnight prior to measurement of gel/melt properties and solids using an Atago E series hand held

refractometer (Gardco, Pompano Beach, FL). The melt temperature was determined by placing a small chunk of the refrigerated gel on a wire string stand held within a test tube so that the chunk does not contact the wall of the test tube. The test tube was covered with aluminum foil with a small hole to allow measurement of the gel temperature using a digital Tempermeter probe. The test tube was immersed in the heating bath so that the chunk is below the surface of a hot water bath at approximately 100°C. A silicone oil bath was used for samples that had melt temperatures above 90°C. The melt temperature was recorded when the gelled sample became wet in appearance, softened and could be stirred (a temperature range was noted). Once the sample had melted, the test tube was transferred to a second beaker containing cold tap water (15°C). The temperature probe was used to record the temperature as the sample was cooled and to probe the sample surface to determine whether the sample had begun to gel. The gel temperature was the temperature upon cooling where the sample no longer flowed to fill in an indentation made by the probe.

The hot sample was then cast, using a draw down bar with a gap set at 3mm clearance, onto 177 mm by 177 mm by 5 mm metal plates which were pre-sprayed with PAM (lecithin) to facilitate easy removal of film material. The gel coated plates were covered to avoid loss of moisture from the cast film. Cast films were typically refrigerated (less than 8°C) for at least one-half hour prior to removal of the film for testing. Refrigeration is not required for film formation. Dried film strips were prepared by drying the coated plates in a 40 °C forced air/fan oven. Films dried 2 hours at 40°C gave an intermediate solids of about 60%, while films dried overnight at 40°C typically gave solids of 80% or higher. Test properties were measured at room temperature

(approximately 20 °C) unless otherwise specified. The percent of solids of the dried film was determined between the cast film at its formulated solids level and the dried film by difference in weight. Break force (BF) was measured on the cast and dried film strips using a Texture Analyzer TA-108S Mini Film Test Rig.

Unless otherwise indicated, Maltrin M100 was obtained from Grain Processing Corporation, Pure-Cote B760 was obtained from Grain Processing Corporation, Sorbitol Special was obtained from SPI Polyols and Glycerin was obtained from VWR (EP/USP grade).

Example 2

Table 8 below shows compositions and film properties for formulations prepared using low viscosity guar ULV 50 in combination with kappa-2 carrageenans.

Cgn A is a kappa-2 carrageenan as defined herein that was obtained as an alkali processed, clarified extract of *Gigartina skottsbergii*, essentially haploid (gametophyte) plants. Minor levels (under 5% total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present. Cgn A has a low divalent cation content and low potassium cation content as shown in Table 7.

Cgn B is a kappa-2 carrageenan that was obtained as an alkali processed, clarified extract of a mixture of *Gigartina skottsbergii* and *Sarcothalia crispata*, primarily haploid (gametophyte) plants. About 10-20% (total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present.

The properties of the kappa-2 carrageenans are shown in Table 7. Viscosity of an aqueous solution at 1.5 wt % solids was measured at 75 °C using a Brookfield LVF

viscometer at appropriate speeds and spindles. The properties of 2% water gels prepared using 2 wt% of samples Cgn A-B (#1) without added cations, (#2) with 0.2 wt% added KCl and (#3) with 0.2% added KCl and 0.2% $CaCl_2$, respectively, were characterized using a TXTM Texture Analyzer. Gels were tested at 25°C and the break force (in grams) and the penetration (in millimeters) was recorded.

Table 7: Properties of Kappa-2 Carrageenan

	Cgn A	Cgn B
Cation Exchange	Yes	No
Mg, %	0.05	0.05
Ca, %	0.15	0.45
K, %	0.67	13.40
Na, %	7.40	0.90
Visc, mPs	98	NT
pH	10.1	"
<u>2% water gel</u>		
BF (g)	0	"
<u>2% water gel (KCl)</u>		
BF(g)	38	"
<u>2% water gel (KCl + $CaCl_2$)</u>		
BF (g)	181	"

Table 8: Formulations and Films Using LV Guar with Kappa-2 Carrageenan

	Ex 2-1	Ex 2-2	Ex 2-3	Ex 2-4	Ex 2-5
Ingredients(g)					
Water	836.3	836.3	836.3	836.3	836.3
Cgn B	0.0	40.5	20.3	0.0	0.0
Cgn A	0.0	0.0	20.3	40.5	40.5
GUAR ULV 50	90.0	49.5	49.5	49.5	49.5
Starch B760	220.8	220.8	220.8	220.8	220.8
Potassium Chloride	0.0	0.0	0.0	4.5	4.5
Sorbitol SP	264.4	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2	88.2

	Ex 2-1	Ex 2-2	Ex 2-3	Ex 2-4	Ex 2-5
Ingredients(g)					
Total weight (g)	1500.0	1500.0	1500.0	1500.0	1500.0
Temp, °C*	90	90	90	87	95
Viscosity, mPa-s*	>50,000	>50,000	>50,000	>50,000	>50.000
Gel, °C	47	68-69	69	50	54-65
Melt, °C	78	85-87	86-88	67-68	76-83
PH	4.8	5.8	5.9	5.2	5.2
Cast film					
Solids, est	42 %	45%	42%	40.2%	45%
BF (g)	<40	239	349	130	330
Dried film (2hr, 40°C)					
Solids, est	65%	60%	60%	63%	66%
BF (g)	722	953	2189	1194	1631
Dried film (16 hr, 40°C)					
Solids, est	86%	87%	75%	84%	84%
BF (g)	4436	7476	6901	6276	8733

*Temperature and viscosity of the molten mass prior to casting

The dried film strength measured after 16 hours, 40 °C for the above inventive gel films is believed to be sufficient to make soft capsules on existing machines. Moreoever, the dried film strength at 2 hours, 40 °C, e.g., of Examples 2-3 to 2-5 also are sufficient to make soft capsules on existing machines. Example 1-2 demonstrates that a 55 to 45 %by weight mixture of guar with kappa-2 carrageenan has increased strength compared to guar alone (Example 2-1). Comparison of Examples 2-4 and 2-5 demonstrates the desirability of maintaining process temperatures for the molten mass above the gel temperature, as Example 2-5 provided finished (dried) gel strengths, when cast at 95 °C, at least 28% higher than a film cast at 87 °C (Example 2-4). The lower gel strength values are reflective of potential pre-gelation during film formation causing a relatively lower gel strength. All films were free of syneresis upon storage and maintained their relative flexibility.

Viscosities were generally found to be at or near the maximum for the test equipment and conditions used. Therefore, use of supplementary equipment with the initial hydration/activation apparatus can provide additional shear and solids concentration effects while maintaining process temperatures well above their high solids set/gel temperatures (> 100°C.). An example of this supplementary equipment, but not limited to, would be an extruder type device sufficient to maintain adequate temperatures and shear necessary to provide the homogeneous mixing and solids concentrations necessary to allow either shaping of the molten mass for direct film or capsule casting or further allow shaping of the molten mass into a desired form such as a film either for use as a film or further processed into other forms and functions.

Example 3

The properties of films prepared by using blend compositions of low viscosity guar gum ULV50 in combination with either kappa carrageenan or kappa carrageenan and/or iota carrageenan are presented in Tables 9 and Table 10, respectively. The carrageenans used are described below. Carrageenan L was a kappa carrageenan having a viscosity of 10-15 cP.

Table 9: Films Using Low Viscosity Guar and Kappa Carrageenan

	Ex 3-1	Ex 3-2	Ex 3-3	Ex 3-4
Ingredient (g)				
Water	836.3	836.3	836.3	836.3
Cgn L	40.5	40.5	40.5	40.5
Guar ULV50	49.5	49.5	49.5	49.5
Starch B760	0	220.8	220.8	0
Starch B790	220.8	0	0	0

	Ex 3-1	Ex 3-2	Ex 3-3	Ex 3-4
Ingredient (g)				
M-100	0	0	0	220.8
KCl	0	0	4.5	4.5
Sorbitol SP	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0
Temp, °C*	90	90	90	90
Viscosity, mPas*	16,000	>50,000	36,750	27,100
As Cast				
Gel, °C	36	53	57	56
Melt, °C	61	75-77	76-78	75-78
pH	5.3	5.2	5.1	5.3
Cast film				
Solids, est	41.5%	40%	45%	43%
BF (g)	170	227 g	283	217
Dried film (2 hrs@ 40C)				
Solids, est	69%	65%	64%	66%
BF (g)	1368	1574	1144	1236
Dried film (16 hours, 40 C)				
Solids, est.	84%	85%	85%	83%
BF (g)	5541	7638	7029	5671

* Temperature and viscosity of the molten mass prior to casting

Use of kappa carrageenan in combination with guar (Example 3-2) increased the film strength for guar alone (Example 2-1).

KCl addition (Example 3-3) increased the gel temperature and also the 40% solids gel strength. Further, KCl addition and varying ratios of film forming ingredients will control cast film strength and gel melt temperatures. When kappa carrageenans are used in combination with low viscosity guar of the invention, control of cation divalency desirably prevents/minimizes gel hardening and brittleness.

Table 10 reports the compositions and properties of films formed using low viscosity guar ULV50 with kappa and iota carrageenans. Cgn C is an alkali processed

clarified kappa carrageenan extract of *Kappaphycus alverezii* (*Eucheuma cottonii*). Cgn D is an alkali processed clarified iota carrageenan extract of *Eucheuma denticulatum* (*Eucheuma spinosum*) with low divalency. Both Cgn C and Cgn D have low divalency.

Table 10: Films Using LV Guar, Kappa Carrageenan, and Iota Carageenans

	Ex 3-5	Ex 3-6	Ex 3-7	Ex 3-8
Ingredient (g)				
Water	836.3	836.5	836.3	836.3
Cgn C	0	13.5	27	40.5
Cgn D	40.5	27	13.5	0
GUAR ULV 50	49.5	49.5	49.5	49.5
Starch B760	220.8	220.8	220.8	220.8
Sorbitol SP	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0
Temp, °C*	93	90	90	90
Viscosity, mPa-s*	46,100	41250	41,500	>50,000
As Cast Film				
Gel, °C	70	46	43	53
Melt, °C	85-90	65-66	56-62	75-77
PH	5.8	5.2	5.4	5.2
As Cast film				
Solids, est	39%	43%	41%	40%
BF (g)	102	48	95	227 g
Dried film (2 hrs@ 40C)				
Solids, est	63 %	60%	60%	65%
BF (g)	1068	282	679	1574
Dried film (16 hours, 40 C)				
Solids, est.	82%	80%	80%	85%
BF (g)	5915	6067	5549	7638

* Temperature and viscosity of the molten mass prior to casting

The above examples show how the addition of the other carrageenans added strength to the low viscosity guar film. Further strengthening and control of gel/melt temperatures can be achieved by adding appropriate amounts of cations.

Example 4

Table 11 presents compositions and properties of films formed using mixtures of guar with potassium alginates and/or carrageenans. Alginates are polyuronate copolymers comprising mannuronate (M) and guluronate(G) units. KAHG is a potassium alginate where the alginate has a high level of G units and is extracted from *Laminaria hyperborean*. KAHM is a potassium alginate where the alginate has a high level of M units and is extracted from *Lessonia nigrescens*.

Table 11: Films using low viscosity Guar, Potassium Alginates and Carrageenans

	Ex 4-1	Ex 4-2	Ex 4-3	Ex 4-4	Ex 4-5	Ex 4-6
Ingredient (g)						
Water	836.3	836.3	836.3	836.3	836.3	836.3
KAHG	60	60	40.5	10.5	0	0
KAHM	0	0	0	0	60.0	10.5
Cgn L	30	30	0	30	30.0	30
GUAR ULV50	0	0	49.5	49.5	0	49.5
Starch B760	220.8	220.8	220.8	220.8	220.8	220.8
Sorbitol SP	264.4	264.4	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0	1500.0	1500.0
Temp, °C*	90	90	88	90	93	92
Viscosity, mPas*	26,500	28,650	24,800	28,250	42,650	31,250
Gel, °C	42	41	50-51	53	39	55
Melt, °C	60-65	62-67	60-61	70-74	60-63	65-69
pH	7.6	7.2	6.3	5.6	7.4	5.9
Cast Film						
Solids, est	40%	40%	40%	40%	38%	41%
BF (g)	<40	<40	<40	188	<40	185
Dried film (2 hrs@ 40°C)						
Solids, est	66%	62%	63%	64%	62%	66%
BF (g)	370	248	445	1811	502	1265

	Ex 4-1	Ex 4-2	Ex 4-3	Ex 4-4	Ex 4-5	Ex 4-6
Ingredient (g)						
Dried film (16 hours, 40 C)						
Solids, est	81%	79%	85%	80%	77%	80%
BF (g)	3826	4253	4144	7960	6918	8301

* Temperature and viscosity of the molten mass prior to casting

Table 12 reports compositions and properties of gel films prepared using blends of low viscosity guar ULV50 with sodium alginates. Protanal® LFR 5/60, Protanal® LF 20/40 and Protanal® SF 120 RB are sodium alginates available from FMC Corporation (Philadelphia, PA).

Table 12: Films Using Guar and Alginates

	Ex-4-7	Ex 4-8	Ex 4-9
Ingredient (g)			
Water	836.3	836.3	836.3
LFR 5/60	40.5	0	0
LF 20/40	0	40.5	0
SF120 RB	0	0	30
GUAR ULV50	49.5	49.5	45
B760	220.8	220.8	220.8
M100	0	0	15.0
Sorbitol SP	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0
Temp, °C*	90	94	93
Viscosity, mPas*	31,650	>50,000	>50,000
Gel, °C	50	NA	NA
Melt, °C	70-71	>95	>93
PH	5.6	5.5	5.6
Cast Film			
Solids, est	40%	40%	40%
BF (g)	<40	102	110
Dried film (2 hrs@ 40°C)			
Solids, est	60%	64%	67%

	Ex-4-7	Ex 4-8	Ex 4-9
Ingredient (g)			
BF (g)	617	1250	1126
Dried film (16 hours, 40 C)			
Solids, est	80%	80%	94%
BF (g)	4780	7701	10,850

* Temperature and viscosity of the molten mass prior to casting

Table 13 presents compositions and gel films formed from low viscosity guar ULV 50 in combination with propylene glycol alginate. Protanal® ester BV4830 and Protanal® ester SLF3 are propylene glycol alginates available from FMC BioPolymer (Philadelphia PA).

Table 13: Films Using Low Viscosity Guar and Propylene Glycol Alginate

	Ex 4-10	Ex 4-11	Ex 4-12	Ex 4-13	Ex 4-14
Ingredient (g)					
Water	836.5	840.3	840.3	840.3	836.3
BV4830	12.0	0	91.2	0	12.0
SLF-3	0	85.5	0	114	0
HEC	0	1.8	1.9	2.4	0
Cgn L	40.5	0	24	0	40.5
GUAR ULV50	37.5	30	0	NONE	37.5
B760	220.8	207.8	207.8	207.8	220.8
M-100	0	0	0	0	
Na citrate	0	2.7	0	3.6	
K citrate	0	0	2.9	0	
KCl	0	0	2.4	0	
Sorbitol SP	264.4	248.8	248.8	248.8	264.4
Glycerin	88.2	83.0	83.0	83	88.2
Temp, °C	90	87	90	91	90
Viscosity, mPas	23,100	16,500	25,000	3250	23,100
Gel, °C	46	34-38	43-46	34-35	46
Melt, °C	60-68	62-64	56-62	58-60	60-68
PH	4.6	4.5	6.3	4.4	4.6

	Ex 4-10	Ex 4-11	Ex 4-12	Ex 4-13	Ex 4-14
Ingredient (g)					
Cast Film					
Solids, est	41.5%	41	45%	39%	41.5%
BF (g)	147	,40	231	<40	147
Dried film (2 hrs@ 40°C)					
Solids, est	60%	65%	55%	74%	60%
BF (g)	592	355	842	1877	592
Dried film (16 hours, 40C)					
Solids, est	80%	77%	78%	85%	80%
Avg film thickness (mm)	0.62	0.60	0.75	0.67	0.62
BF (g)	7214	3317	9599	4677	7214

Example 5

Table 14 lists compositions and properties of gel films prepared using propylene glycol alginate and kappa carrageenan. Protanal® ester BV4830 is a propylene glycol alginates available from FMC Corporation (Philadelphia, PA). HEC is hydroxyethylcellulose. Kappa carrageenan was an alkali processed, clarified extract of *Kappaphycus alaverei* (*Euchema cottonii*). .

Table 14: Propylene Glycol Alginate-based Blend Compositions

Ingredient (g)	5-1	5-2	5-3
Water	840.3	836.3	840.3
BV4830	91.2	49.5	66.0
HEC	1.9		
Kappa cgn	24.0	40.5	54.0
K citrate	2.9		
B760	207.8	220.8	207.8
Sorbitol SP	264.4	264.4	248.8
Glycerin	88.2	88.2	83
Temp, °C*	91	87	89

Ingredient (g)	5-1	5-2	5-3
Viscosity, mPas*	24,800	6550	12500
pH	4.2	3.8	3.9
Gel, °C	59	42-43	43-44
Melt, °C	72-75	54-63	62-64
Cast film			
Solids, est.	45%	38%	36%
BF (g)	136	89	113
Dried @ 16 hours, 40°C			
Solids	87%	79.8	86.6
Avg film thickness (mm)	0.72	0.68	0.79
BF (g)	8838	5244	7638

* Temperature and viscosity of molten mass prior to casting

Table 15 reports compositions and film properties for kappa-2 carrageenan used in combination with propylene glycol alginate and potassium alginate. The kappa-2 carrageenan was an alkali processed, clarified extract of a mixture of *Gigartina skottsbergii* and *Sarcothalia crispata*, primarily haploid (gametophyte) plants. About 10-20% (total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present.

Table 15: Alginate Films With Kappa-2 Carrageenan

	Ex 5-4	Ex 5-5
Ingredient (g)		
Water	834.7	834.7
Kappa-2 Cgn	40.5	54.0
KAHG	31.5	36
BV4830	18.0	36.0
M-100	227.3	227.3
Sorbitol SP	272.2	272.2
Glycerin	90.8	90.8
Temp,°C*	87	84

	Ex 5-4	Ex 5-5
Ingredient (g)		
Viscosity, mPas*	4250	1050
Solids	40	37
Melt,°C	77-78	74-79
Gel,°C	54	52
pH	4.8	5.5
Cast film (est 40% solids)		
BF (g)	142	168
Dried film (est 80% solids) 16 hours, 40C		
Avg film thickness (mm)	0.67	0.48
BF (g)	3409	4004

* Temperature and viscosity of molten mass prior to casting

In example 5-4, potassium cations are supplied by the potassium alginate. The potassium cations promote carrageenan double helix formation at a temperature that allows the carrageenan to form its gel film structure. In example 5-5, the additional strength and lower processing viscosity is believed to be due to the higher level of propylene glycol alginate.

Example 6

As set forth below, Cgn A was obtained as an alkali processed, kappa-2 carrageenan clarified extract of *Gigartina skottsbergii*, essentially haploid (gametophyte) plants and recovered by precipitation with alcohol. Minor levels (under 5% total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present.

Cgn B was obtained by dissolving Cgn A in water, and recovered by alcohol precipitation and drying. Samples of different molecular weights were obtained by

reaction of the dissolved carrageenan with an oxidizing agent to yield Cgn C-F. Sodium hydroxide was added to samples Cgn C-E after the oxidation step and prior to alcohol precipitation to control the pH of the resulting product.

The properties of the kappa-2 carrageenans are shown in Table 16. Viscosity of an aqueous solution at 1.5 wt % solids was measured at 75 °C using a Brookfield LVF viscometer at appropriate speeds and spindles. The properties of 2% water gels prepared using 2 wt% of samples Cgn A-F (#1) without added cations, (#2) with 0.2 wt% added KCl and (#3) with 0.2% added KCl and 0.2% CaCl, respectively, were characterized using a TXTM Texture Analyzer. Gels were tested at 25°C and the break force (in grams) and the penetration (in millimeters) was recorded.

Cgn A-F below are examples of the kappa-2 carrageenans that can be used in the present invention.

Table 16: Properties of Kappa-2 Carrageenans A-F

	Cgn A	Cgn B	Cgn C	Cgn D	Cgn E	Cgn F
Test Oxidization Treatment	No	No	Yes	Yes	Yes	Yes
Mg, %	0.11	0.34	0.19	0.19	0.19	0.19
Ca, %	0.34	0.29	0.34	0.39	0.52	0.40
K, %	12.9	8.46	8.59	8.87	8.74	8.95
Na, %	0.22	0.42	0.51	0.57	0.65	0.38
Visc, mPs*	175	144	48	24	14	11
pH	9.4	9.42	8.93	9.03	9.16	6.7
<u>2% water gel</u>						
BF (g)	211	38	21	18	11	12
Penetration (mm)	7.4	13.9	11.5	9.0	7.8	16.1
<u>2% water gel (KCl)</u>						
BF(g)	308	162	126	107	70	51
Penetration (mm)	7.4	9.9	7.8	7.6	7.3	6.1
<u>2% water gel (KCl + $CaCl_2$)</u>						
BF (g)	487	349	514	445	356	158
Penetration (mm)	3.6	3.1	6.4	5.3	5.0	1.7

* Viscosity measured in 1.5% solids in deionized water at 75°C

In Table 17 below, Cgns D and E were formulated as shown and cast as films. The formulations and film properties are reported in Table II. All formulations are considered to be within the scope of the present invention, though some may be more preferable for a particular use than another.

Table 17. Kappa-2 Carrageenan Formulations and Film Properties

	Ex 6-1	Ex 6-2	Ex 6-3	Ex 6-4
Ingredients(g)				
Water	834.7	834.7	666	497.4
Cgn D	0	75	75	75
Cgn E	75	0	0	0
M-100	227.3	227.3	292.3	357.2
Sorbitol SP	272.2	272.2	349.9	427.7
Glycerin	90.8	90.8	116.8	142.7
Temp, °C*	81.1	82	85	92
Viscosity, mPas*	4000	13,700	22,350	>50,000
Solids (est)	40.1%	40.1%	50.1%	60.0
Gel, °C	55-57	54-55	62	77-78
Melt, °C	73-75	77-80	85	90-92
As cast film				
BF (g)	312	318	404	476
BF (g/mm)	280	303	420	448
Dried film				
(estimated 80% solids) (16 hours @ 40°C)				
Avg film thickness (mm)	1.5	1.0	0.87	1.1
BF (g)	5755	5220	5613	3218

*Temperature and viscosity of the molten mass prior to casting

The above Table shows that in Example 6-2 and Example 6-1, the viscosity of the molten mass at processing temperature (13,700 mPas and 4000 mPas, respectively) was controlled by decreasing the molecular weight of Cgn D to CgnE (expressed as viscosity of 24 mPas and 14 mPas, respectively) with an insignificant impact on film properties.

The melt temperature of the cast material increased (Examples 6-2, 6-3 and 6-4) as the solids content was increased for a given formulation. In Examples 6-2, 6-3 and 6-4, the gel temperature increased with increasing solids until the gel temperature approached the temperature of the molten mass. Gelation, prior to casting, as indicated

by the decreased gel strength of the cast film and the high molten state viscosity (>50,000 mPa) in Example 6-4, is due to the gel temperature approaching the temperature of the molten mass. This indicates the desirability of maintaining the temperature of the molten mass above the gelling temperature during processing if stronger films are desired. Agitation below the gel temperature results in a broken gel structure and decreased strength.

Example 7

Kappa-2 carrageenan was obtained as an alkali processed, clarified extract of a mixture of *Gigartina skottsbergii* and *Sarcothalia crispata*, primarily haploid (gametophyte) plants. About 10-20% (total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants was also present. The extract was recovered and subsequently ion exchanged to provide a kappa-2 carrageenan with low divalency. Properties of the low divalent cation kappa-2 carrageenans (Cgn G-J) are shown in Table 18. Cgn G-J are considered to be within the scope of the invention.

Table 18: Properties of Low Divalent Cation Kappa-2 Carrageenans

	Cgn G	Cgn H	Cgn I	Cgn J
Cation Exchange	Yes	Yes	Yes	Yes
Mg, %	0.07	0.02	0.03	0.05
Ca, %	0.06	0.01	0.16	0.15
K, %	2.19	1.00	0.00	0.67
Na, %	5.12	7.70	6.90	7.40
Visc, mPs	6	18	45	98
pH	8.12	8.7	9.6	10.1
2% water gel				
BF (g)	0	0	0	0
2% water gel (KCl)				
BF(g)	0	13	29	38

	Cgn G	Cgn H	Cgn I	Cgn J
2% water gel (KCl + $CaCl_2$)				
BF (g)	30	93	112	181

Film compositions using the low divalent cation content kappa-2 carrageenans of samples Cgn G-J and the corresponding film properties are presented in Table 19. All formulations below are considered to be within the scope of the present invention, though some may be more preferable for a particular use than another.

Table 19: Films Using Low Divalent Cation Kappa-2 Carrageenan

	Ex 7-1	Ex 7-2	Ex 7-3	Ex 7-4
Ingredients (g)				
Water	834.7	834.7	834.7	834.7
Cgn J	75	0	75	75
Cgn I	0	75	0	0
KCl	0	0	9.0	9.0
Starch B790	0	0	0	227.3
M-100	227.3	227.3	227.3	0
Sorbitol SP	274.9	274.9	274.9	274.9
Glycerin	91.7	91.7	91.7	91.7
Temp,°C*	89	87	87	87
Viscosity, mPas*	5800	5800	6250	10,300
Solids (estimated)	40%	40%	41%	40%
Melt, °C	45-48	43	66-71	70
Gel, °C	35	31	52	48
As Cast Film				
BF (g)	<40	< 40	281	237
Dried film				
Solids, (estimated.~ 80%)				
Avg film thickness	-	-	0.97	0.88

	Ex 7-1	Ex 7-2	Ex 7-3	Ex 7-4
(mm)				
BF (g)	3468	3697	3236	7603

* Temperature and viscosity of the molten mass prior to casting

The ion exchanged kappa-2 carrageenans (I and J) combined with polyols and maltodextrin (as a bulking agent) provided a relatively weaker cast gel film with negligible break force at 40% solids. This is believed to be due to insufficient amounts of potassium cations that are desired to more fully promote carrageenan double helix formation (i.e., gelling) at temperatures that allow the carrageenan to be the primary structuring agent. Examples 7-1 and 7-2 are gel films having relatively lower melt and gel temperatures. Even though gelation potential is not maximized (due to lower potassium levels), Examples 7-1 and 7-2 show a break force of 3468 and 3697, respectively. Example 7-3 demonstrates the effect of potassium ion addition to the structure formed by the kappa-2 carrageenan in Cgn J. Cast strength, although soft, provided sufficient strength for film removal from the casting plate. Structure development by Cgn J, with the addition of potassium ions, is confirmed by the increase in melt and gel temperatures in Example 7-3 as compared to Example 7-1. Break force of the dried film remained comparable to Examples 7-1 and 7-2.

Example 7-4 demonstrates the effect of replacing maltodextrin in Example 7-3 by a modified starch (B790). While viscosity was increased, the gel and melt temperatures remained relatively similar to Example 7-3 which contained the maltodextrin. The cast film strength of Example 7-4 was also relatively equal to Example 7-3. The dried film strength of Example 2-4 was more than doubled as compared to Example 7-3. This clearly indicates the structural synergy between the starch and kappa-2 carrageenan,

when both are present with potassium cations (i.e., gelling ions for kappa-2 carrageenan). Potassium ions may be provided by direct addition of inorganic salts, organic salts, or combinations thereof or contained within additional ingredients. Use of kappa-2 carrageenan containing residual processing salts can promote the desired gel formation conditions that maximizes gel structure and starch synergy. A homogeneous kappa-2 carrageenan/starch gel structure was formed by casting the molten mass at sufficiently high temperatures to prevent pre-gelation.

Additional formulations of the present invention are provided immediately below.

Table 20: Kappa-2 Carrageenan Films

	Ex 7-5	Ex 7-6	Ex 7-7
Ingredients (g)			
Water	834.7	834.7	825
Cgn H	61.4	0	0
Cgn G	0	0	90
Cgn I	0	75.0	0
Calcium sulfate dihydrate	1.7	0	0
Potassium chloride	0	15.0	0
Starch B760	0	0	225
M-100	227.3	227.3	0
Sorbitol SP	275.4	272.2	272.2
Glycerin	91.9	90.8	90.8
Temp, °C*	82	88	75
Viscosity, mPas*	6,500	16,150	18,250
Solids, estimated	39	42	40
Melt, °C	74-77	85	62-65
Gel, °C	56	60-65	42
pH	5.8	6.9	6.9
As Cast Film			
BF (g) at ~40%	338	302	117
Dried 2hrs @ 40C			
BF (g)at ~60%	766	NT	536
Dried 16 hours @ 40°C			
Avg film thickness (mm)	-	0.62	
BF (g) at ~ 80%	3227	4470	6073

NT = not tested

* Temperature and viscosity of the molten mass prior to casting

Example 7-5 was prepared to have equivalent cation content with example 5-1. Both samples show the same gel melt properties. The higher molecular weight of Cgn E (14 cps) in Example 5-1 provided more structural support to the gel film as compared to Cgn H (6 cps) in Example 7-5, as is shown by the higher break force of the dried film. The higher dried film strength of the Example 7-7 shows that use of modified starch in combination with low molecular weight kappa-2 carrageenan provides overall film structure and indicates complexation of kappa-2 carrageenan with the starch.

Example 8

A heated and mixed composition, e.g., any of those in Examples 1-7, is formed into a film in a conventional polymer film casting machine by transferring a controlled thickness of the molten composition onto a temperature controlled rotating drum operated at a temperature such that the film formed is suitable for handling and processing in subsequent operations. Downstream from the film forming operation, films are fed through a series of rollers to counter-rotating dies in a conventional gelatin capsule machine to form, cut and fill capsules of various sizes. During this process, two film surfaces are brought into contact under fusing conditions (i.e., time under sufficient local pressure and local temperature to fuse them together). The formed capsules are discharged for further processing. Recovered capsules have sufficient mechanical strength to withstand handling, packaging, and storage conditions.

Example 9

Soft Capsule Example

Soft gel capsules (7.5 oval) containing mineral oil (Formula A below) were produced using a Technophar SGM1010 soft capsule machine with 7.25 inch long by 4 inch diameter dies. Preparation of the molten mass used to form the capsule shell was as follows: 11.35 lbs of kappa-2-carrageenan was added to a charge of 33.89 lbs of glycerin in a Ross DS40 jacketed vacuum mixer and dispersed at maximum speed for 5 minutes. An additional 11.35 lbs of kappa-2 carrageenan was added to the mixture and dispersed an additional 5 minutes. A premix of 50 lbs of PureCote B790 modified starch in 94.1 lbs of deionized water was then charged to the mixer. The mixer hood was closed and a 26 inch vacuum was pulled to remove air. The contents were mixed for 30 minutes with the planetary mixer at maximum speed and the disperser at 1/3 maximum speed. The vacuum was locked in and the contents of the mixer were then mixed while heating to 90°C by applying low pressure steam (< 10 psig) to the mixer jacket. After reaching a temperature of 90°C, the disperser speed was gradually increased to 2/3 maximum while maintaining the molten mass at a temperature of at least 90°C for 45 minutes. The molten mass was dispensed using a pressurized plate to urge the molten mass to flow as needed from the Ross mixer through a temperature controlled, electrically heated (~125°C) flexible hose to the covered spreader box. The cast films formed in the spreader box were continuous and even. The films were transported by rollers to the capsule forming dies where capsules were formed, filled with mineral oil and sealed. The capsule sealing temperature was 62 °C and the sealing pressure was ~2 bars. The ability to seal was improved as the thickness of the ribbon was decreased from 0.28 inches to

0.16 inches. Capsules were tunnel dried for 72 hours at 80°F and 19% RH. The integrity of the capsule seal remained good after drying. The cast film made from this formulation was dark amber and cloudy with a slight seaweed odor. The break force of the film (0.3 mm in thickness) was 310 g at 58% solids. The breakforce of the film after drying overnight at 40°C and 40% RH (~80% solids) was 3309 g. See A in Table 21 below.

Additional soft capsules (Formula B below) encapsulating mineral oil were produced according to the above process and equipment using a second formulation comprising 39.7 lbs of Sorbitol SP, 59.5 lbs of glycerin, 19.6 lbs of sodium ion exchanged kappa-2 carrageenan, 44.6 Lbs of PureCote B760 starch and 92.6 pounds of water. The Sorbitol SP was added in the starch/water premix. Films produced using this formulation were odorless, transparent and a medium color. The as-cast film had a thickness of 0.6 mm and a break force strength of 263 g at 55% solids. A film sample which was dried overnight at 40°C and 40% RH (~80% solids) had a thickness of 0.7 mm and a breakforce of 6463 g. The as-cast film was more elastic and stretched when fed over the rollers into the capsule dies. Capsules were formed using a capsule seal temperature of 42°C and a seal pressure of 0.5 bar. Mineral oil was encapsulated

The capsules were evaluated for weight, film thickness for each half of the capsule, and burst strength. Burst strength was measured by compressing the capsule to failure. The compression probe had a speed of 1 mm/sec. Ten capsules were tested for each condition. The shell strength is reported as the capsule burst strength with the seam horizontally positioned. The seam strength was measured for 10 capsules with the seam vertically positioned. Results are shown in Table 21. Both kappa-2-carrageenen films were flexible as indicated by the burst distance and produced a strong capsule seal as

indicated by a capsule burst strength that was approximately the same for the capsule shell and the capsule seam and that the capsule did not fail at the seam but at the tip on the seam (away from the point of pressure).

Table 21: Capsule Properties

Capsule Formula	Capsule Weight, (mg)	Film wt/fill weight (mg)	Thickness film1/film2, mm	Shell burst distance Mm	Shell strength, Newtons	Seam burst distance mm	Seam strength, Newtons
Formula A	471	151/320	357/312	6.3	206	6.3	210
Formula B	499	187/312	420/370	5.3	124	5.1	105

While the invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.